REMARKS

I. Status of the Claims

With this amendment, claims 9, 10, 24-40, 42-43, 49-60, 63-66, and 68-75 are pending in the present application and are under examination. Claims 1-8, 11-23, 41, 44-48, 61-62, and 67 have been canceled. Claims 9 and 10 have been amended.

II. Rejections under 35 U.S.C. §103(a)

The Examiner has rejected claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-52, 54-60, 63-66, and 68-75 as allegedly being unpatentable over Shiver *et al*, Haas *et al.*, Persson *et al.*, and Novitzky *et al.*

The Examiner has rejected claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-60, 63-66, and 68-75 as allegedly being unpatentable over Shiver *et al*, Haas *et al.*, Novitzky *et al.*, and Persson *et al.*, as applied to claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-52, 54-60, 63-66, and 68-75, in further view of March *et al.*

The Examiner has rejected claims 9, 10, 24-40, 42, 43, 49-52, 54-60, 63-66, and 68-75 as allegedly being unpatentable over Shiver *et al*, Haas *et al.*, Novitzky *et al.*, and Persson *et al.*, as applied to claims 9, 10, 24-29, 33, 39, 40, 42, 43, 49-52, 54-60, 63-66, and 68-75, in further view of Kapitonov *et al.* The Examiner alleges that based on the teachings of Shiver *et al.* and Schneider *et al.* it would have been obvious to one of skill in the art to eliminate any "ATTTA" sequences, wild-type or modified.

Applicant respectfully traverses each of the rejections and their supporting remarks. A *prima facie* obviousness action has not been established. The Examiner has asserted that Shiver *et al.* teach the removal of INS sequences by pointing to the statement in Shiver *et al.* regarding removal of "ATTTA" sequences. While this may constitute removal of INS sequences, this does not correspond to the changes made as per Figure 5. The removal of inhibitory sequences did not involve direct elimination of any "ATTTA" sequences. In the application is stated on page 26, lines 22-24, that "highly expressed human codons prefer nucleotides G or C. The Gag coding sequences were modified to be comparable to codon usage found in highly expressed human genes." And further on page 26, lines 25-29 and page 27, line 1 it reads that "Second,

there are inhibitory (or instability) elements (INS) located within the coding sequences of the Gag coding sequences. The RRE is a secondary structure that interacts with the HIV encoded Rev-protein to overcome the expression down-regulating effects of the INS. To overcome post-transcriptional activating mechanisms of RRE and Rev, the instability elements can be inactivated by introducing multiple point mutations that do not alter the reading frame of the encoded proteins." Figure 5 in the application demonstrates the changes (boxed frames) in the nucleic acid coding sequence of the Gag gene by removal of the instability elements ***after*** the AT-rich wild-type codons had been replaced with those of GC-rich highly expressed human genes. The resulting sequence by implementation of both methods as disclosed in the application is shown in Figure 1 (SEQ ID NO: 3) and is clearly different from the sequence one would get if only either of the methods were applied. Furthermore, the changes made in Figure 5 do not appear to be the changes referred to in Shiver *et al.* ("ATTTA") as most of the changes do not involve As or Ts. Therefore, the Examiner's reference to Shiver *et al.* teaching of changing ATTTA does not appear to constitute a teaching or suggestion to make the changes to the sequences made as shown Figure 5.

Furthermore, even if it were obvious to optimize the Gag coding sequences for improved expression, there are many ways to improve expression of genes which will change the nucleic acid sequence, including, but not limited to, selecting codon usage from differently efficient expressed genes from a variety of species; modifying the codon usage of the whole gene or only a fraction thereof; complete or incomplete removal of inhibitory sequences, internal signal sequences, and splicing signals; implementing various start and stop codon sequence environments; and the order of execution of these nucleic acid sequence modifications. In addition, there are many possible strains from which an HIV type C Gag coding sequence may be obtained besides those that the inventors chose, which could also affect the final modified sequence.

Thus, the resulting sequences as disclosed in SEQ ID NOs: 3 and 4 are not obvious, since although the amino acid sequence of the HIV Gag protein was previously disclosed, the potential number of nucleic acid sequences for increased expression of the HIV Gag protein is representing a broad genus given that one of skill in the art could have selected from a significant number of different type C Gag coding sequences as of the priority date and one of skill in the art

could have chosen from a number of different optimization techniques, each of which could have generated a different optimized sequence. Thus, even if it were obvious to optimize an HIV type C Gag coding sequence, that would not render SEQ ID NOs: 3 or 4 obvious as SEQ ID NOs: 3 and 4 are species of the genus of possible optimized HIV type C Gag coding sequences. See, e.g., *In re Deuel*, 51 F.3d 1552, 1558-59, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995), where the Federal Circuit stated, "[a] prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein." The present situation is analogous as there are many possible optimized HIV type C Gag encoding sequences, while the instant claims are directed to two particular polynucleotide sequences – SEQ ID NOs: 3 and 4.

Since the Examiner has not shown that the obviousness rejections teach or suggest the optimization as shown in Figure 5, and even if optimization of an HIV type C Gag encoding sequence were obvious, the pending claims are a species of such optimized coding sequences and are therefore not obvious over the genus of optimized coding sequences. Applicants therefore respectfully request withdrawal of the three rejections under 35 U.S.C. 103(a) of claims 9, 10, 24-40, 42-43, 49-60, 63-66, and 68-75 under 35 U.S.C § 103(a).

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 223002109700. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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